Primary retroperitoneal squamous cell carcinoma: a case report with review of the literature

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Abstract

Squamous cell carcinoma originating in the retroperitoneal cavity is an exceedingly rare disease, and little is known about it. Here, we report the case of primary retroperitoneal squamous cell carcinoma. A 76-year-old gravida four para two woman with a history of hysterectomy for unknown reasons was referred to our hospital for an infant-head-sized multicystic pelvic mass. She was initially diagnosed with ovarian cancer Stage IIB, poorly differentiated carcinoma by exploratory laparotomy in which only a tumor biopsy was performed due to severe adhesion. She underwent 5 courses of combination chemotherapy with paclitaxel and carboplatin, which reduced the tumor from 14 to 6.5 cm. Interval debulking surgery proved that the tumor was in the retroperitoneal cavity and not associated with the ovaries. She was finally diagnosed with squamous cell carcinoma originating in the retroperitoneal cavity. Human papilloma virus type 16 was identified using polymerase chain reaction. Three more courses of paclitaxel and carboplatin were administered, and she has been without evidence of disease for 6 months. A comprehensive literature search identified seven similar cases of which four individuals had a history of abdominal hysterectomy. Four out of the seven cases were tested for the presence of P16, two for HPV; all the results were positive. These findings suggest that HPV could be the cause of squamous cell carcinoma on the pelvic peritoneum, and that past hysterectomy is a possible contributing factor.

Keywords Retroperitoneal cancer · Squamous cell carcinoma · Human papilloma virus

Introduction

Primary retroperitoneal neoplasms that arise within the retroperitoneum but outside the major organs are rare and estimated to represent approximately 0.1–0.2% of all malignant tumors [1]. Most frequent entities include lymphoproliferative tumors, soft tissue tumors and extragonadal germ cell tumors, but diagnosis of these tumors is often challenging [1]. Squamous cell carcinoma (SCC) originating in the retroperitoneal cavity is exceedingly rare, and only several cases were reported in the past [1–4]. Some of these cases were

reported as squamous cell carcinoma of unknown primary. Little is known about its pathogenesis and clinical feature, therefore the optimal treatment is unclear. Here we report the case who was diagnosed as SCC caused by human papilloma virus infection and possibly arising in retroperitoneal cavity.

Case report

A 76-year-old gravida four para two woman with a past history of abdominal hysterectomy for unknown reasons visited her local doctor with a chief complaint of anal pain. A cystic mass was revealed in the pelvic cavity by plain computed tomography (CT) scanning. She was introduced to our hospital for further examination and treatment. Gynecological pelvic examination identified an infant-head-sized cystic mass on the upper left of the vaginal stump. A 10 cm in diameter cystic lesion with solid components was found in the left pelvic cavity by transvaginal ultrasonography (Fig. 1). Tumor markers including carcinoembryonic antigen (CEA), carbohydrate antigen 125 (CA125), and carbohydrate antigen

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Fig. 1 A 10-cm-diameter cystic lesion with solid components that was found in the left pelvic cavity using transvaginal ultrasonography

19–9 (CA19–9) were negative, but SCC was 2.3 ng/ml which was slightly elevated. Contrast magnetic resonance imaging (MRI) showed a 14-cm cystic tumor in the longest diameter with enhanced solid components and septal walls in the left pelvic cavity (Fig. 2a–c). No other lesions were identified through CT scanning. CT scanning showed that the tumor was supplied by the left ovarian artery, so primary ovarian epithelial cancer was suspected at this point.

We performed an exploratory laparotomy in which only a part of the tumor could be seen and bilateral ovaries

could not be identified due to severe adhesion. There was only a small amount of ascites, and no dissemination was identified. Only tumor biopsy was conducted, and pathologically it showed atypical cells growing in nests with interstitial invasion, which suggested poorly differentiated carcinoma, undifferentiated SCC, or malignant Brenner tumor (Fig. 3a, b). The patient was initially diagnosed with ovarian cancer stage IIB. Five courses of paclitaxel and carboplatin reduced the tumor size from 14 to 6.5 cm in diameter, and interval debulking surgery was performed. During surgery, we found that the tumor was in the retroperitoneal cavity and strongly adhered to the left ovary, bladder and sigmoid colon. It also involved the left ureter within it. Adhesiolysis revealed that the left ovary appeared normal, whereas the right ovary was absent which suggested that it had been removed in the previous operation. Pathologically, polygonal squamous cells were growing in nests, intervening desmoplastic stroma (Fig. 3c, d). The component of teratoma, Brenner tumor, urothelial carcinoma or endometrioid carcinoma was not identified. Most of the tumor was intraepithelial lesion, and metastatic carcinoma was not indicated. Immunohistochemistry revealed positive for P16, and human papilloma virus (HPV) type 16 was identified when 16 types of HPV (type 6, 11, 16, 18, 30, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, and 66) were surveyed using polymerase chain reaction. She was finally diagnosed with squamous cell carcinoma arising in the retroperitoneal cavity. Three more courses of paclitaxel and carboplatin were administered. SCC level decreased to the normal range within 1 month after operation, and she has been without evidence of disease for 6 months.

Fig. 2 MRI showed a 14-cm cystic tumor on the longest diameter with enhanced solid components and septal walls in the left pelvic cavity. **a** T2WI, **b** T1WI, and **c** enhanced T1WI

Fig. 3 **a** Microscopic findings of the tumor biopsy taken during the exploratory laparotomy revealed atypical cells growing in nests with interstitial invasion, which suggested poorly differentiated carcinoma, undifferentiated SCC, or malignant Brenner tumor. 40× magnification. **b** 200× magnification. **c** Microscopic findings of the resected

tumor by interval debulking surgery showed that polygonal squamous cell grow in nests, intervening desmoplastic stroma. 20× magnification. **d** Immunoreactive staining was positive for P16. 20× magnification

Discussion

SCC of the pelvic retroperitoneum is exceedingly rare, with limited data regarding its origin, management, and prognosis. We conducted a literature review using PubMed and found that six cases were reported before as pathological SCC derived in the retroperitoneal cavity (Table 1) [1–4]. Among these seven cases including our case, the average age was 61 years old, and four individuals had a history of abdominal hysterectomy. Six of the seven patients had some pain in their lower body as a chief complaint. CT or ultrasound guided biopsy was performed to make a diagnosis in three cases, and the other four cases underwent exploratory laparotomy. The average maximum diameter was 6.2 cm. The tumor was in the retroperitoneal cavity in all cases, but information about positional relation of the tumor and vagina or vaginal stump was not found. Four out of the seven cases were tested for the presence of P16, and two for HPV, all the results were positive. As a treatment, tumor resection was conducted in four patients, and they received either

combination chemotherapy or chemoradiation. One patient died because of the disease within 1 year after the operation, but the other three are alive without disease (follow-up 0–4 years). Two of the three other patients who did not receive surgery had metastasis in pelvic lymph nodes. They underwent concurrent chemoradiation therapy and are alive with no evidence of disease (follow-up 0 and 7 months). The last patient opted not to receive any treatment and died of the disease 1 year after diagnosis.

The diagnosis of retroperitoneal tumors is often challenging. In our case, the patient was diagnosed with ovarian cancer at first, and we finally found during the operation that the tumor was in the retroperitoneal cavity. In our review, CT or ultrasound guided biopsy tended to be chosen as a diagnostic modality when there were metastatic lesions in pelvic lymph nodes. In three cases in which there were no other lesions, exploratory laparotomy was needed.

The etiology and pathogenesis of retroperitoneal SCC are unclear. The previous report said that it might arise from squamous metaplasia of preexisting embryonic rests, which

Table 1 Seven cases of retroperitoneal squamous cell carcinoma

Case	Age (years)	Past Ob/Gyn history	Chief complaint	Location of the tumor	Tumor size	Metastasis	Diagnostic modality	Immunostaining	Treatment	Outcome	References
1	56	–	None (regular check-up)	Left retroperitoneal parametrium	5.5 cm	Left pelvic lymph nodes	Exploratory laparotomy	P16(+) HPV18(+)	Tumor resection + PeN → 5-FU/CDDP	Under treatment	[1]
2	64	Supracervical hysterectomy (unknown indication)	Lower abdominal pain	Near the left greater sciatic foramen	5 cm	Left pelvic lymph nodes	CT-guided biopsy	–	TC → CCRT	Under treatment	[2]
3	69	TAH + BSO (benign lesion)	Left femoral pain	Left-sided retroperitoneal mass	2.7 cm	Left pelvic lymph nodes	CT-guided biopsy	P16(+)	CCRT (CDDP)	NED 7 months	[3]
4	58	TAH + BSO (endometriosis)	Left hip pain	Left retroperitoneal cavity	7 cm	–	Exploratory laparotomy	P16(+)	Tumor resection → CCRT (CDDP)	NED 4 years	
5	47	–	Left leg pain	Left-sided retroperitoneal mass	7.4 cm	Para aortic lymph node	Ultrasound guided biopsy	P16(+)	Opted not to receive any treatment	DOD 1 year	
6	57	–	Pelvic pain, constipation	Right rectovaginal septum	6 cm	–	Exploratory laparotomy	–	Tumor resection + TAH + BSO → 5-FU/CDDP	DOD 6 months	[4]
7	76	TAH (unknown indication)	Anal pain	Left retroperitoneal cavity	10 cm	–	Exploratory laparotomy	P16(+) HPV16(+)	TC → tumor resection + left PeN → TC	NED 6 months	Our patient

TAH total abdominal hysterectomy, BSO bilateral salpingo-oophorectomy, Ob/Gyn obstetrical or gynecological, HPV human papilloma virus, PeN pelvic lymphadenectomy, 5-FU fluorouracil, CDDP cisplatin, TC paclitaxel and carboplatin, CCRT concurrent chemoradiation therapy, NED no evidence of disease, DOD dead of disease

is thought to be the consequence of chronic peritoneal irritation [5]. Recently, Isbell et al. and Oh et al. [1, 3] reported HPV-related retroperitoneal squamous cell carcinoma. Four cases were reported in their literature, and P16 was positive in all cases and HPV18 in one case. HPV is a common cause of genital, gynecologic and anal cancers with rates of 50% for vulvar cancers, 64–91% for vaginal cancers, 95% for cervical cancers, and 90% for anal cancers [6]. HPV is usually thought to infect cells in these regions by direct exposure. In regions other than genital or oropharyngeal tissue, for example bladder, prostate, esophagus and lung, HPV may be spread directly through external genitals or the oral cavity. The route of transmission of HPV to the retroperitoneal cavity has not been elucidated. Clements et al. reported five cases of SCC in psoas and one case of SCC in pelvic lymph node [7]. P16 was positive in all cases, and they proposed that hematogenous or lymphatic spread of HPV might explain the findings, or microscopic cervical disease that could not be detected by current screening or that had resolved at the primary site might be the origin. In our review, four of the seven cases had a past history of abdominal hysterectomy. The positional relation of the tumor and vagina or vaginal stump and cervical HPV status before hysterectomy were not described. In these four cases, it is possible that HPV infected cervical or vaginal cells or HPV itself spread to the retroperitoneal cavity during hysterectomy. It is also possible that latent HPV on the vagina may have been involved when vaginal stump was sutured and may have infiltrated the retroperitoneal space.

Treatment of SCC of the pelvic retroperitoneum has not been established yet. For localized cervical SCC which is also related with HPV infection, either operation or radiation can bring equal treatment effects [8]. In the case of anal SCC, local excision is recommended for early stage, but radiation therapy is also important for the case with inadequate margins or locally advanced cases. Considering either operation or radiation is recommended for those cancers that are usually caused by HPV, perhaps retroperitoneal SCC can be sensitive to radiation therapy. In our review, surgery or chemoradiation seemed to achieve favorable prognosis. However, long-term clinical courses were not reported thoroughly, and further follow-up is needed.

In conclusion, HPV could be the cause of SCC on the pelvic peritoneum, and past hysterectomy may be a contributing

factor. Surgery or chemoradiation may be useful as treatment, but further follow-up is needed.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. For this type of study formal consent is not required.

Informed consent Informed consent was obtained from the participant included in the study.

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